prevalence should be offered or advised to seek HIV counseling and testing.

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The New Progestins

IN AN EFFORT TO DECREASE androgenic side effects, combination oral contraceptive pills have undergone a further refinement. New oral contraceptive formulations are available containing one of these 19-nortestosterone progestins: desogestrel, norgestimate, or gestodene. While other progestin preparations are still available, these new ones have less binding affinity to the androgen receptor and decrease androgen-mediated metabolic changes, weight gain, acne, and hirsutism. When compared to other low-dose—not more than 35 μg ethinyl estradiol—combination oral contraceptive pills, these new formulations were comparable in efficacy, the incidence of breakthrough bleeding, and the absence of withdrawal menses. They had less effect on carbohydrate and lipoprotein metabolism than currently used oral contraceptives. No difference was seen in the incidence of thromboembolic events or an increase in blood pressure with the new progestins.

Before their introduction in the United States, these progestins were extensively tested in Europe. Studies reported increased levels of sex hormone-binding globulin with an associated decrease in free testosterone levels after new progestin use. While all combination oral contraceptives have the ability to decrease androgen-mediated side effects, the new progestins offer clinically proved improvement of acne and hirsutism. With respect to carbohydrate metabolism, women using desogestrel- and gestodene-containing oral contraceptives had small increases in the area under the glucose curve, determined during an oral glucose tolerance test. In comparison, norgestimate formulations caused no changes in carbohydrate metabolism. When compared for their effect on lipid metabolism, new progestins increased high-density lipoprotein (HDL) levels and decreased low-density lipoprotein (LDL) levels to a greater extent than most currently used oral contraceptives. Subtle differences, however, exist among the new progestins. Desogestrel preparations produced the largest average increase (12.9%) in HDL levels, while desogestrel and gestodene formulations were associated with the largest average decrease (2.1% to 2.5%) in LDL levels. All three new progestins increased triglyceride levels (range, 14.8% to 38.3%), with norgestimate and gestodene demonstrating the minimal and maximal average increases, respectively.

Desogestrel-containing oral contraceptive pills are available currently as a monophasic preparation (Desogen, Ortho-Cept) for clinical use. Norgestimate-containing oral contraceptive pills are also available as a monophasic (Ortho-Cyclen) and triphasic (Ortho Tri-Cyclen) progestin preparation. Where competing pharmaceutical companies are producing similar products, there may be a distinct difference in the selling price of the medication. Additional formulations (a gestodene-containing and a desogestrel triphasic preparation) are currently being reviewed by the US Food and Drug Administration. The oral contraceptives are packaged in both standard 21- and 28-day regimens. New progestins have a comparable or longer half-life than current progestins, which minimizes the effect of a missed or late pill ingestion. These medications represent a good initial choice for the first-time oral contraception user.

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Laparoscopically-Assisted Hysterectomy

THE USE OF THE LAPAROSCOPE during hysterectomy has generated much interest and controversy. Terms such as "laparoscopically-directed hysterectomy," "laparoscopically-assisted vaginal hysterectomy," and "laparoscopic hysterectomy" are often used interchangeably and represent a spectrum of laparoscopic procedures. Diagnostic laparoscopy before standard vaginal hysterectomy may help surgeons detect unsuspected pelvic pathology. Operative laparoscopy is used to treat conditions that would have prevented a safe vaginal approach ("directed") or to "assist" the hysterectomy by doing some of the dissections, ligations, and incisions laparoscopically that would have otherwise been done vaginally. Total laparoscopic hysterectomy involves the complete laparoscopic ligation of uterine blood supply and supporting ligaments. The surgical steps are the same as for abdominal hysterectomy, but the uterus is usually delivered vaginally.

The laparoscopic approach has potential advantages over standard vaginal hysterectomy. It allows safer and better adnexal surgical procedures when benign ovarian pathology is present, provides better uterine descensus and thus facilitates vaginal surgical procedures, offers better pelvic overview both before and after a surgical procedure, and allows lysis of adhesions and treatment of endometriosis. It can also be used to treat other pelvic conditions. The main advantage of this procedure is its potential ability to convert many abdominal cases into vaginal ones. There has been concern about the potential risks of complications and increased anesthesia and operating time. In expert hands, however, this procedure rarely exceeds two hours, and current series have not reported

higher rates for these operative complications. There have been reports of ureteric injuries, postoperative bleeding, and hematomas with the use of endoscopic staple devices.

The nature of this new technique has ethical, medicolegal, and economic ramifications. Whether the laparoscopic procedure is going to replace a good number of abdominal surgical procedures is uncertain at this time. Early reports have shown that in expert hands the immediate morbidity, mortality, and postoperative course of these procedures are comparable to their vaginal counterparts and better than their abdominal ones. Numbers are still limited, and there are no long-term follow-up studies. An important concern is whether these numbers represent a bias because published reports have mostly come from expert laparoscopists. Retrospective analysis of 50 laparoscopically-assisted vaginal hysterectomy procedures done in a residency setting indicate that perioperative complications occur in 12% of patients, compared to 26% for abdominal hysterectomy and 6% for vaginal hysterectomy. The most common complications were febrile morbidity, abdominal wall ecchymosis, and intraoperative bleeding requiring transfusion, occurring in 4%, 4%, and 6% of patients, respectively. All these complications were managed conservatively. With laparoscopically-assisted vaginal hysterectomy procedures, hospital costs (about $10,000) are comparable to those with abdominal hysterectomy (about $12,000) but notably higher than for vaginal hysterectomy (about $8,000).

Laparoscopically-assisted hysterectomies are technically difficult and developing the necessary skills is typically associated with a slow learning phase. We recommend that procedures be done with the assistance of an experienced surgeon until one feels comfortable without supervision. Appropriate proctoring is important.

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Assisted Reproductive Technology

SUCCESS RATES FOR ASSISTED reproductive technology continue to improve and availability has become widespread. More than 33,000 cycles of treatment are initiated annually, with delivery rates ranging from 15% to 27% per retrieval. Improvements in embryo freezing have further increased overall success. More than 4,800 frozen embryo transfers resulted in an additional 11% delivery rate per transfer.

The growth of assisted reproductive technology has accelerated research efforts in all aspects of reproduction. This relates particularly to bettering the understanding of spermatogenesis, oocyte maturation, fertilization, preembryo growth and development, and implantation. Exciting and innovative developments have occurred with respect to micromanipulation for the treatment of male infertility; the application of oocyte donation to women of advanced reproductive age; and the reexamination of the unstimulated cycle and its value to in vitro fertilization.

In men, 40% of infertility results from abnormalities in gamete production. In vitro fertilization success rates have been low in these couples compared to patients with tubal disease. An inability to fertilize oocytes represents the greatest problem these men encounter. Pregnancies and births following micromanipulation have been reported in men previously unable to fertilize, using procedures such as partial zonal dissection, subzonal insemination, and most recently intracytoplasmic sperm injection. In experienced hands, pregnancy rates as high as 30% per embryo transfer and, more impressively, 22% of retrieval cycles have been reported following the application of intracytoplasmic sperm injection.

Oocyte donation to women of advanced reproductive age (older than 40 years) has opened up therapy to a new subset of patients. Success measured by implantation rates, clinical pregnancy rates, and, most important, delivery rates in recipients between the ages of 40 and 60 years have been no different from that of their younger counterparts. Presently more than 1,000 oocyte donation cycles are done annually. The method involves synchronizing young, fertile oocyte donors undergoing controlled ovarian hyperstimulation and transvaginal ultrasound-directed follicle aspiration and hormonally prepared functionally agonadal recipients. Delivery rates are typically reported between 25% and 40% per embryo transfer. Guidelines published by the American Fertility Society should aid the practitioner in selecting appropriate candidates for treatment.

Combining assisted reproductive technology and a patient's own natural cycle has reemerged. Pregnancy rates per retrieval are highest when using controlled ovarian hyperstimulation. There are disadvantages related to the high cost of medications, the need for expensive surveillance methods, and the multiple birth rate that follows the transfer of supernumerary embryos, however. Unstimulated cycles take less time, are less traumatic, are less expensive, and result in singleton pregnancies. Pregnancy rates per retrieval are lower using unstimulated in vitro fertilization (28% versus 14%); the embryo implantation rates are actually higher (13% versus 9%), however. Accordingly, life-table analysis indicates that two to three cycles of unstimulated in vitro fertilization yield the same likelihood of pregnancy as a single cycle of controlled ovarian hyperstimulation. Given the reduced cost of the unstimulated approach, repetitive attempts on an individual basis become reasonably cost-effective.

As illustrated by the above examples, assisted reproductive technology now includes multiple measures to treat patients once considered hopelessly infertile. Successful resolution of a patient's infertility warrants careful attention to the treatment plan and the appropriate selection of various approaches.

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